4:15

913-2 Ageing and the Molecular and Structural Remodelling of Cardiac Extracellular Matrix During β-Adrenergic Stimulation

S. Masson, B. Arosio, F. Fiordaliso, N. Gagliano, D. Santambrogio, L. Calvillo, R. Latini, G. Annoni. *Istituto "Mario Negri" and IRCCS Ospedale Maggiore, Milan, Italy*

Background: The capacity of the aged heart to adapt to work overload by compensatory responses is debated. Accordingly, we compared the molecular and structural remodelling of the myocardial extracellular matrix of old and young rats in response to short-term infusion of a β-adrenergic agonist.

Methods: Male Wistar rats aged 3- (young) or 18 months (old) were infused for 3 d with isoproterenol (ISO, 1 mg/kg/d) by implanted osmotic minipumps or untreated (control). The mRNA abundance of ANP, α_2 (I) (COL-I) and α_1 (III) (COL-III) procollagens, TGF-β1, TGF-β3 and SPARC (Secreted Protein Acidic and Rich in Cysteine, a glycoprotein with anti-adhesive properties) genes in LV were evaluated by Northern and Dot blot analyses while collagen accumulation in LV interstitium and around coronary arteries was measured with an automated image analyser after Sirius red staining.

Results: ISO infusion raised HR by around 80 bpm in either young or old animals and provoked similar increase of LV weight (+38% *vs.* +44% in young versus old rats, 2-way ANOVA: NS interaction). The messenger abundance of ANP was increased 2.8 and 2.7-fold by ISO in LV from young and old rats, respectively. Transcripts of SPARC, COL-III, TGF-β_1 and TGF-β_3, but not COL-I, increased similarly in each age group. Interstitial collagen density was significantly higher in old than in young controls, but it reached similar levels after ISO infusion (4.83 ± 0.49 *vs.* 4.89 ± 0.46% of LV area). Perivascular fibrosis increased independently of age.

Conclusion: LV from aged rats has preserved the capacity to adapt to sustained β-adrenergic stimulation by undergoing a process of remodelling - hypertrophy and fibrosis - comparable to that observed in younger animals.

4:30

913-3 Age-associated LV Remodeling in Normal Men and Women Detected by 3D MRI

P.S. Hees, J.L. Fleg, J.L. Weiss, S.L. Bosley, E.G. Lakatta, E.P. Shapiro. *Johns Hopkins University and Gerontology Research Center, NIA, Baltimore, MD, USA*

Echocardiographic (echo) LV wall thickness increases with normative aging, suggesting global LV hypertrophy (LVH). However, autopsy studies have shown no change, or an actual decrease, in LV mass with age, especially in men. To investigate this apparent discrepancy, we studied 3D structural changes of the LV with aging using MRI, in 160 normal subjects (83 female and 77 male, ages 21–93) in the Baltimore Longitudinal Study of Aging, carefully screened for the absence of hypertension and coronary disease. In each subject, LV mass (M) was determined from a series of short axis slices using Simpson's rule, and LV apex-to-base length (L), regional wall thickness (WT), and diameter (D), were measured. Also, 2D-derived M-mode echo was used to measure WT and D in a random subset of 80 subjects, and M derived by a standard ASE algorithm. L, WT, and D were indexed to height, and mass to BSA.

In women, MRI-WT increased by about 20% over the age range studied ($r = 0.27$, $p < 0.05$) while MRI-L tended to decrease by about 9% ($r = -0.19$, $p = 0.10$), and MRI-D was unchanged ($r = -0.14$, $p = 0.25$). As a result, MRI-M did not vary with age ($r = -0.04$, $p = 0.06$). In men, MRI-WT and MRI-D were unchanged ($r = 0.04$, $p = 0.81$; $r = 0.09$, $p = 0.48$, respectively), but there was an 9% fall in MRI-L ($r = -0.33$, $p < 0.004$), resulting in a 12% decrease in MRI-M over the age range studied ($r = -0.25$, $p < 0.04$). Echo-M did not vary with age in either gender, although echo-WT increased in both.

Therefore, advancing age is accompanied by a gender-dependent remodeling of the LV, which, in women tends to shorten as the wall thickens, without a change in overall mass, but in men shortens without a change in wall thickness with reduced overall mass. The LV thus becomes more spherical with advancing age. These changes, which require 3D data to detect, may contribute to the reduced functional reserve in the elderly.

4:45

913-4 Quantitative Evaluation of Changes in Global Left Ventricular Shape Associated With Aging in the Absence of Heart Disease

G. Mirra, K. Ogunyankin, E. Avelar, D. Galzerano, D. Lama, M. Vannan, N. Pandian. *Tufts - New England Medical Center, Boston, MA, USA*

It is known that aging is associated with preservation of end-diastolic volume as well as global systolic function, and a progressive increase in relative LV wall thickness. The effect of these on global LV shape in a normal elderly population is not known. We hypothesized that the LV in the aged undergoes remodeling to a more spherical shape in order to preserve LV volume and function. Using 2D echo, we studied 19 elderly subjects aged 75 ± 8 yrs (65–91) and 13 healthy subjects aged 28 ± 3 yrs (24–32). None had significant heart disease, hypertension, LVH, CHF or coronary disease. The end-systolic (es) and end-diastolic (ed) endocardial contours (apical LAX) view were digitized and processed using a proprietary Fourier shape analysis software. The Fourier Power index (PI) and the F3 component in end-diastole and end-systole in the aged were compared to that in the young. Higher PI (unitless) represents a more elliptical ventricle, while a lower value represents a more spherical ventricle. The F3 component (unitless) is a measure of elongation, an index corrected for ventricular size.

Results:

	Young	Elderly	p
Mean EF %	55 ± 7	58 ± 4	0.11
PIed	18 ± 1.06	14.2 ± 1.33	0.01*
PIes	34.5 ± 3.4	21.7 ± 3.1	0.002*
F3ed	0.37 ± 0.13	0.33 ± 0.02	0.07
F3es	0.5 ± 0.03	0.33 ± 0.03	0.0005*

We conclude that the LV geometry shows a more round shape deformation with increasing age in the absence of overt heart disease, and these changes are more pronounced in systole.

914 Special Topics in Acute Myocardial Infarction Therapy: Strokes and Calcium Channel Blockers

Wednesday, April 1, 1998, 4:00 p.m.–5:00 p.m.
Georgia World Congress Center, Room 261W

4:00

914-1 Comparison of Stroke Rates in Patients With Acute Coronary Syndromes and Patients With Acute Myocardial Infarction

K.W. Mahaffey, R.A. Harrington, C. Graffagnino, M.J. Alberts, M.A. Sloan, J.M. Miller, C.B. Granger, M.L. Simoons, E.J. Topol, R.M. Califf. *Duke Clinical Research Institute, Durham, NC, USA*

Background: The risk for stroke in patients with acute myocardial infarction (MI) treated with thrombolysis is well characterized but the incidence in patients with unstable angina/non-Q wave MI is less certain.

Methods: To compare the stroke rates in these two patient populations we analyzed data from GUSTO-I (N = 41,021) and data from the PURSUIT trial of 10,948 patients evaluating low-dose (N = 1487) and high-dose (N = 4722) glycoprotein IIb/IIIa inhibition compared with placebo (N = 4739) in patients with unstable angina/non-Q wave MI.

Stroke Type	PURSUIT		GUSTO-I
			All patients
Intracranial hemorrhage	3 (0.1%)	3 (0.1%)	268 (0.7%)
Non-hemorrhagic	34 (0.7%)	27 (0.6%)	247 (0.6%)

Results: The intracranial hemorrhage rate was low in the absence of thrombolytic therapy. The rates for non-hemorrhagic stroke were similar despite patients in PURSUIT being slightly older (median age, 64 vs 62), more often female (35% vs 25%), and with a higher incidence of hypertension (55% vs 38%), prior MI (32% vs 16%), and prior stroke or transient ischemic attack (4% vs 2%) compared with the GUSTO-I population.

Conclusion: Intracranial hemorrhage is not increased with use of IIb/IIIa inhibition, while non-hemorrhagic stroke is observed in patients across the entire spectrum of acute coronary syndromes.

4:15

914-2 The Rate of Ischemic Stroke Following Acute Myocardial Infarction Is Decreasing. The National Registry of Myocardial Infarction Experience

M.A. Sloan, S.R. Pirzada, J.P. Ornato, J.H. Gurwitz, J.M. Gore, A.J. Tiefenbrunn, W.J. French, W.D. Weaver, W.J. Rogers. *For the NRMI-2 participants University of Maryland; Baltimore, Maryland, USA*

Background: Little descriptive information exists on the rate of and outcome from ischemic stroke (IS) following acute myocardial infarction (AMI) outside randomized clinical trials.